

***Remarks***

Claims 85-124, 126, 127, and 135-140 are canceled herein without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in continuing applications. New claims 141-164 have been added. Support for the new claims can be found, *inter alia*, at page 8, line 19, through page 10, line 6 of the instant specification. No new matter has been added by way of this amendment. Claims 141-164 are pending in the application.

**I. *Claim Objections***

Claim 139 is objected to for being of improper dependent form for failing to further limit the subject matter of the parent claim. (Office Action, page 2.) Claim 139 is canceled herein rendering this objection moot.

**II. *Rejection of the claims under 35 U.S.C. § 112, second paragraph***

Claims 85-124, 126, 127, and 135-140 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. (Office Action, page 3.) Specifically, the Examiner maintains that claim 85 is indefinite since one of skill in the art cannot determine the metes and bounds of the term “substantially equal” relative mass, that the term “base pairs” cannot refer to single stranded nucleic acids, the term “plurality of fragments” is unclear and that the manner in which the relative mass is calculated is not clear.

Applicants respectfully disagree with the Examiner however, to expedite prosecution, claims 85-124, 126, 127, and 135-140 have been canceled without prejudice or disclaimer. In view of this cancellation, and the language of the new claims submitted herein, the rejection of these claims under 35 U.S.C. § 112, second paragraph, is moot.

**II. *Rejection of claims under 35 U.S.C. §§ 102 and 103***

Claims 85-101, 103-121, 123, 124, 127, and 135-140 stand rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Carlson *et al.* (U.S. Patent No. 5,316,908). (Office Action, page 5.) Applicants respectfully disagree.

The Examiner asserts that Figure 1 of Carlson *et al.* discloses a nucleic acid ladder that meets the size, relative mass, and intensity requirements of claims 85-101, 103-121, 123, 124, 127, and 135-140. (Office Action, page 5.) Claims 85-101, 103-121, 123, 124, 127, and 135-140 have been canceled herein and replaced by new claims 141-164.

New independent claim 141 recites in part “a plurality of double stranded nucleic acid fragments, each fragment having a size in base pairs, a copy number, a mass, and a relative mass wherein the mass of each fragment is the size in base pairs of the fragment multiplied by the copy number of the fragment, wherein the relative mass of each fragment is the mass of the fragment divided by the sum of the masses of all of the fragments, wherein the relative mass of the fragments of the plurality are substantially equal.” In conjunction with the description of substantially equal mass given in the specification at page 9, lines 8-10 and dependent claims 161-164 which recite specific ranges for a substantially equal mass, Applicants believe that the new claims are in compliance with 35 U.S.C. § 112, second paragraph. Further, Applicants believe that the new claims, when properly construed, require a reconsideration of the prior art.

The Examiner acknowledges that the prior claims were directed to a nucleic acid ladder composition, and were not limited by an electrophoretic system or a requirement that the ladder be stained, or be allowed to fluoresce. (Office Action, page 5.) The Examiner goes on to assert that the properties of a composition do not impart patentability to the composition if the composition itself is old, and that the claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art. Further, the Examiner asserts that the metes and bounds of the term “substantially equal mass” are unclear. However, Applicants assert that the present claims do recite a physical property that differentiates them from the prior art. Claim 141 recites, in part, that the relative mass (a physical property) of the nucleic acid fragments of each size is substantially equal.

Carlson *et al.* fails to disclose this relationship amongst the nucleic acid fragments. As noted at column 2, lines 21-23 of Carlson *et al.*, “FIG. 1 is a schematic scale drawing of how the first and second molecular marker kits would migrate on an electrophoretic gel.” One skilled in the art would recognize that a schematic drawing of an electrophoretic gel would not convey any information beyond how different sized bands migrate on the gel. Applicants assert that such a diagram does not convey any information on intensity of staining, copy number or total mass of the nucleic acid present in any individual band. Further, Carlson *et al.* alters the copy number of

the largest and the smallest fragments in the ladder by increasing their copy number relative to the copy number of the middle range fragments (column 5, lines 55-63 of Carlson *et al.*). This alteration is described by Carlson *et al.* as one that overcomes the poor hybridization efficiency of the larger fragments and the poor retention of the smaller fragments on a membrane. If one were to increase the copy number of the larger fragments relative to the medium sized fragments (as described by Carlson *et al.*), both the relative mass and the total mass of the larger fragments would be increased in comparison to other fragments in the ladder. Because the claims prosecuted herein require that the relative mass (claim 141) of each fragment in the ladder be substantially equal, Carlson *et al.* fails to disclose all of the limitations of these claims.

In addition, as discussed above, the increase in copy number of the larger fragments compared to the medium-sized fragments would lead to an increase in the relative mass or the total mass of the larger fragments, rather than a mass that is substantially equal as claimed herein. Applicants have demonstrated in Figure 2 of the instant application that several commercially available nucleic acid ladders meet this size requirement. However, neither this figure or the other ladders disclosed in Figure 2, describe the relative mass requirements recited in the instant claims. Figure 1 of Carlson *et al.* merely lists a range of nucleic acid fragments, irrespective of the relative mass of each of those fragments. Furthermore, as evidenced by the multitude of commercially-available DNA ladders disclosed in Figure 2 of the specification that fail to meet this requirement, the need had not been met in the art. Thus, the Examiner has failed to provide a *prima facie* case of obviousness.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a).

***Conclusion***

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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